Commissioner of Food and Drugs concludes that in order for the labeling of such drugs to bear adequate information for their safe use, as required by § 201.100, such labeling must include the following:

Warning: Occasional patients have been reported to develop severe paradoxical airway resistance with repeated, excessive use of isoproterenol inhalation preparations. The cause of this refractory state is unknown. It is advisable that in such instances the use of this preparation be discontinued immediately and alternative therapy instituted, since in the reported cases the patients did not respond to other forms of therapy until the drug was withdrawn.

Deaths have been reported following excessive use of isoproterenol inhalation preparations and the exact cause is unknown. Cardiac arrest was noted in several instances.

(c)(1) The Commissioner also concludes that in view of the manner in which these preparations are self-administered for relief of attacks of bronchial asthma and other chronic bronchopulmonary disorders, it is necessary for the protection of users that warning information to patients be included as a part of the label and as part of any instructions to patients included in the package dispensed to the patient as follows:

Warning: Do not exceed the dose prescribed by your physician. If difficulty in breathing persists, contact your physician immediately.

(2) The warning on the label may be accomplished (i) by including it on the immediate container label with a statement directed to pharmacists not to remove the label or (ii) by including in the package a printed warning with instructions to pharmacists to place the warning on the container prior to dispensing.

(d) The marketing of isoproterenol inhalation preparations may be continued if all the following conditions are met:

(1) Within 30 days following the date of publication of this section in the FEDERAL REGISTER:

(i) The label and labeling of such preparations shipped within the jurisdiction of the act are in accordance with paragraphs (b) and (c) of this section.

(ii) The holder of an approved new-drug application for such preparation submits a supplement to his new-drug application to provide for appropriate labeling changes as described in paragraphs (b) and (c) of this section.

(2) Within 90 days following the date of publication of this section in the FEDERAL REGISTER, the manufacturer, packer, or distributor of any drug containing isoproterenol intended for inhalation for which a new-drug approval is not in effect submits a new-drug application containing satisfactory information of the kinds required by § 314.50 of this chapter, including appropriate labeling as described in paragraphs (b) and (c) of this section.

(3) The applicant submits additional information required for the approval of the application as may be specified in a written communication from the Food and Drug Administration.

(e) After 270 days following expiration of said 90 days, regulatory proceedings based on section 505(a) of the Federal Food, Drug, and Cosmetic Act may be initiated with regard to any such drug shipped within the jurisdiction of the act for which an approved new-drug application is not in effect.

[40 FR 13998, Mar. 27, 1975, as amended at 55 FR 11576, Mar. 29, 1990]

§ 201.306 Potassium salt preparations intended for oral ingestion by man.

(a) The Food and Drug Administration will initiate no regulatory action with respect to the continued marketing of coated tablets containing potassium chloride or other potassium salts which supply 100 milligrams or more of potassium per tablet provided all the following conditions are met:

(1) Within 30 days from the date of publication of this statement of policy in the FEDERAL REGISTER:

(i) The labeling of the drug bears the prescription caution statement quoted in section 503(b)(4) of the Federal Food, Drug, and Cosmetic Act;

(ii) The labeling on or within the package from which the drug is to be dispensed bears adequate information for its use by practitioners in accord with the ''full disclosure'' labeling requirements of § 201.100 of this chapter, including the following warning statement:

Warning—There have been several reports, published and unpublished, concerning nonspecific small-bowel lesions consisting of stenosis, with or without ulceration, associated with the administration of enteric-coated thiazides with potassium salts. These lesions may occur with enteric-coated potassium tablets alone or when they are used with nonenteric-coated thiazides, or certain other oral diuretics. These small-bowel lesions have caused obstruction, hemorrhage, and perforation. Surgery was frequently required and deaths have occurred. Based on a large survey of physicians and hospitals, both United States and foreign, the incidence of these lesions is low, and a causal relationship in man has not been definitely established. Available information tends to implicate enteric-coated potassium salts, although lesions of this type also occur spontaneously. Therefore, coated potassium-containing formulations should be administered only when indicated, and should be discontinued immediately if abdominal pain, distention, nausea, vomiting, or gastrointestinal bleeding occur. Coated potassium tablets should be used only when adequate dietary supplementation is not practicable.

(Although the warning statement includes references to enteric-coated potassium salt preparations, it applies to any capsule or coated tablet of a potassium salt intended for oral ingestion without prior dilution with an adequate volume of liquid to preclude gastrointestinal injury.)

(iii) Any other labeling or additional advertising for the drug conforms to the labeling described in paragraph (a)(1)(ii) of this section, in accordance with §§ 202.1 and 201.100 of this chapter.

(2) Within 90 days from the date of publication of this statement of policy in the FEDERAL REGISTER, the manufacturer, packer, or distributor of the drug shall submit a new-drug application containing satisfactory information of the kind required by § 314.50 of this chapter, with appropriate labeling as described in this paragraph.

(b) The Food and Drug Administration may initiate regulatory proceedings after 30 days from the date of publication of this section, with respect to the marketing of uncoated tablets containing potassium chloride or other potassium salts which supply 100 milligrams or more of potassium per tablet or with respect to liquid preparations containing potassium chloride or other potassium salts which supply 20 milligrams or more of potassium per milliliter, labeled or intended for human use, unless all the following conditions are met:

(1) The labeling of the drug bears the prescription caution statement quoted in section 503(b)(4) of the Federal Food, Drug, and Cosmetic Act; and

(2) The labeling on or within the package from which the drug is to be dispensed bears adequate information for its use by practitioners in accord with the ''full disclosure'' labeling requirements of § 201.100 of this chapter, including a recommendation that patients be directed to dissolve any such tablets in an appropriate amount of liquid and to dilute any such liquid preparations adequately to assure against gastrointestinal injury associated with the oral ingestion of concentrated potassium salt preparations.

[40 FR 13998, Mar. 27, 1975, as amended at 55 FR 11576, Mar. 29, 1990]

§ 201.308 Ipecac syrup; warnings and directions for use for over-the-counter sale.

(a) It is estimated that each year about 500,000 accidental poisonings occur in the United States and result in approximately 1,500 deaths, of which over 400 are children. In the emergency treatment of these poisonings, ipecac syrup is considered the emetic of choice. The immediate availability of this drug for use in such situations is critical, since rapid treatment may be the difference between life and death. The restriction of this drug to prescription sale limits its availability in emergencies. On the other hand, it is the consensus of informed medical opinion that ipecac syrup should be used only under medical supervision in the emergency treatment of poisonings. In view of these facts, the question of whether ipecac syrup labeled as an emergency treatment for use in poisonings should be available over the counter has been controversial.

(b) In connection with its study of this problem, the Food and Drug Administration has obtained the views of medical authorities. It is the unanimous recommendation of the American Academy of Pediatrics, the American Association of Poison Control Centers, the American Medical Association, and